

A Convenient Nitroxide Radical Synthesis

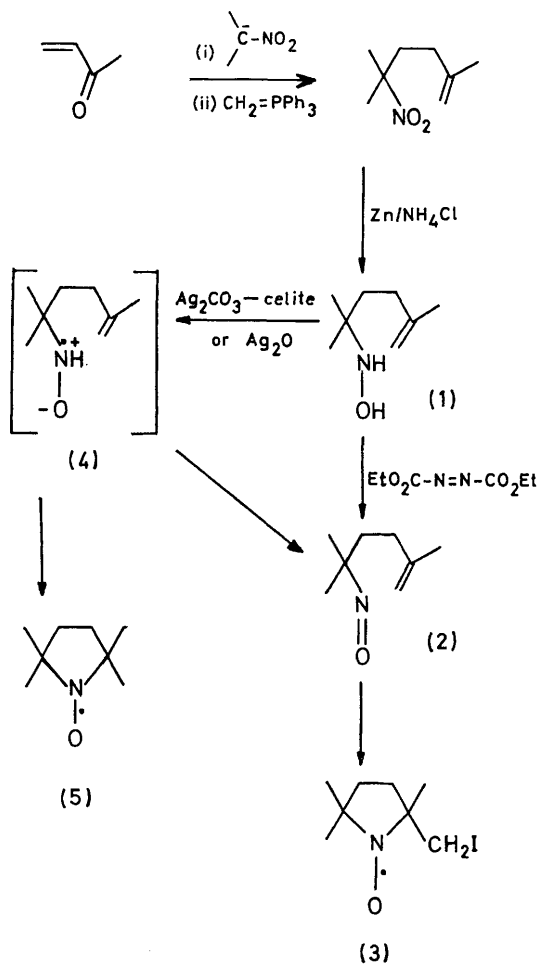
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Summary A number of suitably substituted $\delta\epsilon$ -unsaturated nitroso-compounds have been prepared and cyclised to pyrrolidino-nitroxide radicals.

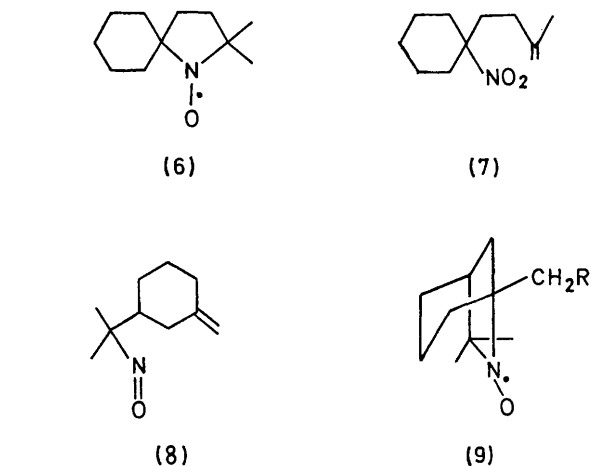
SOME time ago we described the ready formation of a stable nitroxide radical by treatment of an appropriately substituted nitroso-olefin with iodine.¹ We have now

$g = 2.0064$] in 6% yield after column chromatography. The low yield can be ascribed to two major factors: (i) the oxidation (Ag_2CO_3 -celite² or Ag_2O) of the hydroxyamino-olefin (1) does not generate the desired nitroso-olefin (2) exclusively. By column chromatography we have been able



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examined this general type of reaction using the simpler substrate (2) which is readily prepared as outlined in the Scheme. Treatment of (2) with iodine in chloroform gives the pure iodo-nitroxide (3) as a yellow-orange liquid [M^++1 269, M^+ 268; e.s.r. (CHCl_3) triplet $a_N = 13.6$ Oe,



to isolate the parent nitroxide (5)§ in 20% yield. The exact mechanism of formation of this compound is uncertain but we suggest that the precursor is the monoalkyl nitroxide (4)³ which can undergo cyclisation in a manner analogous to certain olefinic aminium radical cations.⁴ This is partially substantiated by the fact that no trace of (5) is observed when the oxidation of (1) is accomplished with diethyl azodicarboxylate,⁵ a reaction which converts a hydroxylamine into a nitroso-compound by a presumed concerted process. (ii) It has been shown that the nitroso-olefin (2) is itself rather unstable and readily undergoes intramolecular 'ene' cyclisation.⁶

Similarly, the spiro-nitroxide (6) m.p. 29–31.5°, [e.s.r. (Et_2O) triplet $a_N = 13.9$ Oe, $g = 2.0070$] is prepared in 30% yield from the nitroso-olefin (7). We have also demonstrated that the stable nitroso-olefin (8) (dimer m.p. 77–79°), readily affords the bicyclo-[3,2,1] iodo-nitroxide (9, $\text{R} = \text{I}$) (m.p. 96°, [M^++1 295, M^+ 294; e.s.r. (CHCl_3) triplet $a_N = 14.4$ Oe, $g = 2.0072$] in 40% yield which can be converted into the very volatile liquid nitroxide (9, $\text{R} = \text{H}$) [M^++1 169, M^+ 168; e.s.r. (CHCl_3) triplet $a_N = 15.6$ Oe, $g = 2.0071$] by Raney nickel reduction followed by re-oxidation of the resultant amine.

This process represents a bifurcated approach to the synthesis of pyrrolidino nitroxide radicals. Preliminary results indicate that the scope of this reaction may also be extended to the piperidino-class. Furthermore, we antici-

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‡ A strong M^++1 peak is a mass spectral characteristic of nitroxide radicals, E. F. J. Duynstee, M. E. A. H. Mevis, H. K. Ostendorf, and R. J. de Kock, *Rec. Trav. Chim.*, 1968, **87**, 945; A. Morrison and A. P. Davies, *Org. Mass Spec.*, 1970, **3**, 353.

§ This compound is identical to an authentic sample.

pate that the use of other radical initiators or nucleophilic displacement of I^- will augment the versatility of the overall sequence. e.s.r. data and one of us (W.B.M.) gratefully acknowledges receipt of a Carnegie Trust Grant.

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¹ D. M. Hawley, J. S. Roberts, G. Ferguson, and A. L. Porte, *Chem. Comm.*, 1967, 942. For a recent review of nitroxide radical syntheses see, E. G. Rozantsev and V. D. Sholle, *Synthesis*, 1971, 190.

² J. A. Maassen and Th. J. de Boer, *Rec. Trav. Chim.*, 1971, 90, 373.

³ For references to these species see Th. A. J. W. Wajer, A. Mackor, and Th. J. de Boer, *Tetrahedron*, 1969, 25, 175.

⁴ G. Esposito, R. Furstoss, and B. Waegell, *Tetrahedron Letters*, 1971, 895, 899; J.-M. Surzur, L. Stella, and R. Nougier, *Tetrahedron Letters*, 1971, 903; Y. L. Chow, R. A. Perry, and B. C. Menon, *Tetrahedron Letters*, 1971, 1549.

⁵ E. C. Taylor and F. Yoneda, *Chem. Comm.*, 1967, 199.

⁶ W. B. Motherwell and J. S. Roberts, Following Communication.